Remarks

Prior to entry of the Amendment Claims 1-25 were pending in the present application with claims 1-5 and 8-25 withdrawn from consideration as being drawn to a non-elected invention. Applicants reserve the right to prosecute the originally filed, broader, and/or similar claims in one or more additional applications and do not waive any of their rights or abandon any non-elected subject matter. With this amendment, Claims 6 and 7 are amended. Claims 26-29 are newly added. Support for the amendments and new claims is found in the specification as originally filed, see for example paragraph 66-67 and Table 1. The amendments and the various rejections raised in the Office Action are discussed in more detail below.

Rejection under 35 C.F.R. §112 first paragraph: enablement

Claims 6 and 7 stand rejected under 35 C.F.R. §112, first paragraph as allegedly failing to comply with the enablement requirement. Applicants traverse the rejection.

According to the MPEP Section 2164.04, in order to make a rejection, the Patent Office has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention. *In re* Wright, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). A specification disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of 35 U.S.C. §112, first paragraph, unless there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support. (*See*, MPEP Section 2164.04).

Applicants submit that the claims satisfy the enablement requirement for the follow reasons. Claim 6, as amended, recites a variant *H. jecorina* CBH1 cellulase, wherein said variant comprises a substitution or deletion at a position corresponding to T66 of the mature *H. jecorina* CBH1 protein (SEQ ID NO. 2), wherein said variant *H. jecorina* CBH1 cellulase has cellulolytic activity and the variant is encoded by an nucleic acid sequence that hybridizes to a nucleic acid sequence having about 80% sequence identity to (SEQ ID NO: 1). Dependent Claim 7 is directed to variant *H. jecorina* CBH1 cellulase according to Claim 6, wherein said variant comprises a substitution at a

position corresponding to a residue selected from the group consisting of Q186(E), S195(A/F), E239S, G242(H/Y/N/S/T/D/A) and P412(T/S/A). As the specification discloses, Applicants have identified possible sites involved in the stability of the CBH1 enzyme in three different ways based on alignment of the sequences of the homologs with CBH1. In the first method, sites that differed between the *H. jecorina* CBH1 catalytic domain and the catalytic domain of at least one of the homologs of lower stability (*i.e.*, excluding only *H. orientalis*) were identified as possible sites involved in the thermostability of CBH1. The sites identified included, *inter alia*, the sites presently claimed in Claim 6 (T66) and Claim 7 (Q186, S195, E239, G242, P412) in CBH1 from *H. jecorina*. In the second method, sites where the residue in *H. jecorina* or *H. orientalis* is the same as that found in all of the decreased stability enzyme homologs resulted in the identification of sites that lacked correlation with T_m. Again, the specification describes that the sites identified as retaining relevance with stability included, *inter alia*, the sites presently claimed in Claim 6 (T66) and Claim 7 (Q186, S195, E239, G242, P412) in CBH1 from *H. jecorina*. In the third method described in the specification, sites where *H. jecorina* and *H. orientalis* are the same, with the corresponding residue in *H. schweinitzii* being either the same or different as in either of these two, but a different amino acid in the corresponding site of either *T. konilangbra* or *T. pseudokoningii* were considered as possible sites involved in thermostability of the enzyme. The sites identified included, *inter alia*, the sites presently claimed in Claim 7 (Q186, S195, and P412) in CBH1 from *Hypocrea jecorina*. Finally, the specification teaches the variant CBH1 polypeptides comprise a substitution or deletion at a position corresponding to one or more of residues, including, *inter alia*, the sites presently claimed in Claim 6 (T66) and Claim 7 (Q186, S195, E239, G242, P412) (*See*, specification, paragraph [0208]).

Applicants assert that a specification which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of under 35 C.F.R. §1.12 first paragraph, unless there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support. (*See*, MPEP, Section 2164.04). In addition, Applicants assert that a person of ordinary skill in the art reading Applicants specification at the time it was filed would have been able to make and use

the presently claimed invention. This is particular true given the level of skill in the art and the teaching of Applicants' specification. For example, Figure 2 of Applicants specification provides an alignment of 5 CBH1 homologs. The alignment indicates which regions are conserved. As described above, Applicants have identified possible sites involved in the stability of the CBH1 enzyme in three different ways based on alignment of the sequences of the homologs with CBH1. A person of ordinary skill in the art would readily have been able use standard methods to make the cellulases containing the substitutions or deletions at the claimed sites, particularly since the examples of such methods are set forth in Applicants specification.

Finally, the Patent Office maintains that undue experimentation would be required to produce active proteins with the claimed changes. (*See*, Office Action, page 3). Applicants respectfully remind the Patent Office that compliance with the enablement requirement of 35 U.S.C. 112, first paragraph does not turn on whether an example is disclosed. In fact, the specification need not contain an example if the invention is otherwise disclosed in such manner that one skilled in the art will be able to practice it without an undue amount of experimentation. *In re* Borkowski, 422 F.2d 904, 164 USPQ 642 (CCPA 1970). Because only an enabling disclosure is required, applicant need not describe all actual embodiments. (*See*, MPEP, Section 2164.02). Although the variants would need to be assayed for activity, the present Specification provides the means to conduct the assay. (*See*, Specification, paragraph [0283], and Example 2 paragraphs [0343]-[0344]. Simply requiring additional testing (the methods for which are provided in the Specification itself, does not render the Claims non-enabled. There is indeed an expectation of success, through the use of the assay methods provided in the Specification. Indeed the present specification explicitly teaches the variant CBH1 polypeptides comprise a substitution or deletion at a position corresponding to one or more of residues, including, *inter alia*, the sites presently claimed in Claim 6 (T66) and Claim 7 (Q186, S195, E239, G242, P412) (*See*, specification, paragraph [0208]) and teaches how to assess the activity of the enzyme.

In light of the above, Applicants respectfully submit that the rejection of Claims 6 and 7, under 35 U.S.C. 112§, first paragraph, enablement has been overcome and respectfully request reconsideration and withdrawal of the rejection.

Rejection under 35 C.F.R. §112, first paragraph: written description.

Claims 6 and 7 stand rejected under 35 C.F.R. §112, first paragraph as allegedly failing to comply with the written description requirement. Applicants traverse the rejection.

Under Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1563-64, (Fed. Cir. 1991), to satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention, and that the invention, in that context, is whatever is now claimed. Possession of the claimed invention may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was "ready for patenting" such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention. (*See*, MPEP 2163.02, citing Pfaff v. Wells Elecs., Inc., 525 U.S. 55, 68, (1998); Regents of the University of California v. Eli Lilly, 119 F.3d 1559, 1568 (Fed. Cir. 1997); Amgen, Inc. v. Chugai Pharmaceutical, 927 F.2d 1200, 1206, 1021 (Fed. Cir. 1991) (one must define a compound by "whatever characteristics sufficiently distinguish it").

Applicants respectfully submit that variant CBH1 cellulases comprising a substitution or deletion at the claimed positions of the mature *H. jecorina* CBH1 protein is supported by the specification as filed. In particular, the specification teaches the variant CBH1 polypeptides comprise a substitution or deletion at a position corresponding to one or more of residues, including, *inter alia*, the sites presently claimed in Claim 6 (T66) and Claim 7 (Q186, S195, E239, G242, P412) (*See*, specification, paragraph [0208]). Simply because the claims arguably encompass a large number of variants, is not a proper ground for rejection, as the present specification provides the teaching necessary to obtain and assay the claimed CBH1 variants.

Although Applicants must respectfully disagree with the Examiner's argument and rationale, in order to further the prosecution of the present application and Applicants' business interests, yet without acquiescing to the Examiner's arguments, Applicants have amended Claim 6 and 7 to more clearly describe what the Applicants

consider the invention. In light of the above remarks, Applicants respectfully request withdrawal of the rejection Claims 6 and 7, under 35 U.S.C. 112§, 112, first paragraph, written description.

Rejections Under 35 U.S.C.§ 102(b)

Claim 6 stands rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by either of von der Osten, *et al.*, Schulein, *et al.*, Miettinen-Oinonen, *et al.*, or Lund *et al.* Applicants respectfully traverse the rejection.

Anticipation of a claim is met "only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. Applicants assert that the amendments made herein render the 35 U.S.C.§ 102(b) rejections moot.

Applicants respectfully submit that SEQ ID NO:1 in von der Osten *et al.* is a endoglucanase from *Myceliophthora thermophila* (see, von der Osten, U.S. Patent No. 5,912,157, col. 11, lines 14-15) and the sequence alignment provided by the Patent Office indicates only a 28% query match. Likewise, SEQ. ID. NO: 11 in Schulein, *et al.*, is directed to the amino acid sequence of an endoglucanase from *Myceliophthora thermophila* (SEQ ID NO:11) (see, Schulein, *et al*, U.S. Patent No. 6,117,664, col. 9. lines 18-20) and the sequence alignment provided by the Patent Office indicates only a 27.8% and 27.4% query match. SEQ ID NOs: 33 and 35 in Schulein, *et al.*, is directed to the amino acid sequence of *Melanocarpus albomyces* (SEQ ID NO:11) (see, Miettinen-Oinonen, *et al.* U.S. Patent No. 6,184,019) and the sequence alignment provided by the Patent Office indicates only a 27.6%, 44.5% and 44.6% query match. In addition, SEQ ID NO:1-3 in Lund, *et al.* are directed to the amino acid sequence of *Humicola insolens*. (see, Lund, *et al.* U.S. Patent No. 6,261,828) and the sequence alignment provided by the Patent Office indicates only a 27.0%, 27.4% and 26.9% query match.

Thus, in contrast to the cited art, instant Claim 6 is directed to a variant *H. jecorina* CBH1 cellulase, wherein said variant comprises a substitution or deletion at a position corresponding T66 of the mature *H. jecorina* CBH1 protein (SEQ ID NO: 2) and the variant is encoded by a nucleic acid sequence that hybridizes to a nucleic acid

sequence having about 80% sequence identity to (SEQ ID NO: 1). As such, the cited art does not disclose each and every element of Claim 6, as required to anticipate the claim. Accordingly, reconsideration and withdrawal of the rejection of Claim 6, under 35 U.S.C. § 102(b) is respectfully requested.

Claims 6 and 7 stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Radford, *et al.* Applicants traverse the rejection.

SEQ ID NO:3 in Radford, *et al.* is directed to the amino acid sequence of *H. grisea*, and SEQ ID NO:2 is directed to the amino acid sequence of *Neurospora crassa* (see, Radford, *et al.* U.S. Patent No. 5,955,270) and the sequence alignments provided by the Patent Office indicates only a 60.1%, 57.0% and 60.5% query match.

Thus, in contrast to Radford *et al.*, the instant claims 6 and 7 are directed to a variant *H. jecorina* CBH1 cellulase, wherein said variant comprises a substitution or deletion at a position corresponding to T66 of the mature *H. jecorina* CBH1 protein (SEQ ID NO. 2) and the variant is encoded by a nucleic acid sequence that hybridizes to a nucleic acid sequence having about 80% sequence identity to (SEQ ID NO: 1). As such, Radford, *et al.* does not disclose each and every element of Claim 6 and Claim 7, as required to anticipate the claims. Accordingly, reconsideration and withdrawal of the rejection of Claims 6 and Claim 7, under 35 U.S.C. § 102(b) is respectfully requested.

Although Applicants must respectfully disagree with the Examiner's argument and rationale, in order to further the prosecution of the present application and Applicants' business interests, yet without acquiescing to the Examiner's arguments, Applicants have amended Claim 6 and 7 to more clearly describe what the Applicants consider the invention. Accordingly, reconsideration and withdrawal of the rejection of Claims 6 and Claim 7, under 35 U.S.C. § 102(b) is respectfully requested.

Conclusion

In light of the above amendments, as well as the above remarks, Applicants believe the pending claims are in condition of allowance and issuance of a Notice of Allowance is respectfully requested. If a telephone conference would expedite prosecution of the application, the Examiner is invited to telephone the undersigned at (650) 846-7614.

Respectfully submitted,

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